UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/867,924	05/30/2001	Blake J. Roessler	UM-06191	7554

72960 7590 11/28/2007

Casimir Jones, S.C.
440 Science Drive
Suite 203
Madison, WI 53711

EXAMINER	
FUBARA, BLESSING M	
ART UNIT	PAPER NUMBER
1618	

MAIL DATE	DELIVERY MODE
11/28/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/867,924	ROESSLER ET AL.	
	Examiner	Art Unit	
	Blessing M. Fubara	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 March 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25,26,28-42,45-55 and 65* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25, 26, 28-42, 45-55 and 65* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Examiner acknowledges receipt power of attorney, request for reconsideration and remarks filed 9/13/07. Claims 25, 26, 28-42, 45-55 and 65 are pending.

Response to Arguments

Previous rejections that are not reiterated herein are withdrawn.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 25, 26, 28-42, 45-55 and 65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Foldvari et al. ("Cutaneous vaccination: the skin as an immunologically active tissue and the challenge of antigen delivery," in Journal of Controlled Release, Volume 66, Issues 2-3, 15 May 2000, Pages 199-214) and Baker et al. ("Regulation of in vivo gene expression using antisense oligonucleotides or antisense expression plasmids transfected using starburst PAMAM dendrimers," in Nucleic Acids Research, 1996, Vol. 24, No. 11, pp 2176-2182) in view of Park et al. (US 6,267,987).

3. Foldvari discloses transdermal delivery of protein or nucleotide to the skin tissue (pp. 71-86). Foldvari discloses on page 205 that dendrimers are known to deliver DNA. Foldvari discloses cutaneous vaccination (title). The skin (paragraph 2) through which the vaccine is administered meets the limitation of skin tissue cells of the claims. Foldvari discloses dendrimers that are complexed with DNA in spherical structures and the dendrimers and the DNA can be delivered to cell lines (right column, first full paragraph of page 205). Acrylate, PAMAM and polyethyleneimine polymers are some of the polymers listed that are used with the DNA (right column, page 205). Furthermore, Foldvari discloses the use of PLGA, PLA, lactides and glycolides for delivery of protein, carbohydrate or DNA vaccines (right column, page 204). These polymers are biocompatible and biodegradable. Liposomes are also used to deliver beneficial agents (paragraph 3.4). DNA oligonucleotide meets nucleic acid of the claims.

Regarding claim 26, Baker describes transfer of oligonucleotides in cell culture (abstract). Baker discloses the use of PAMAM dendrimers for effective delivery of oligonucleotides evaluated in vitro cell culture system (abstract, right column of page 2177). Park discloses polyester based dendrimer system for delivery of oligonucleotides (abstract; column 2, lines 3-5, 36-40; column 3, lines 24-34; column 4, lines 1-46; column 9, lines 8-17). Baker discloses the use of dendrimers to deliver DNA (pp 2176-2182).

Regarding biocompatible membrane of claim 32, 33 and 35, Foldvari describes microencapsulation in polyester membranes (microspheres, liposomes) and the polyesters are bioerodible. Regarding the collagen of claim 36, it would be obvious to substitute one membrane material for another and still expect effective delivery of the nucleotides. For

example, collagen is an essential protein, which can be found in skin, connective tissue, blood vessels, bone and other parts of the body and collagen and PLGA have been used as membrane materials with dendrimer to deliver DNA (see abstract of Bielinska et al. "Application of membrane-based dendrimer/DNA complexes for solid phase transfection in vitro and in vivo" in Biomaterials, Vol.21, Issue 9, May 2000, pages 877-997, as a teaching reference).

The DNA meets the requirement of claims 25 and 45 as biological agent that is nucleic acid..

Wound healing, encoding growth factor are all functions of DNA; protein that comprises protein that promotes tissue vascularization is the function of the protein. Thus claims 46, 47, 48, 49, 51, 52, 53 and 54 are met.

Therefore, the motivation to combine the references flows from teaching in the references that oligonucleotides are deliverable by dendrimers that are composed of polyesters (Foldvari and Park) and expected to successfully deliver the nucleotides to the tissues that are contacted with the dendrimer (abstract of Baker). Therefore, the cited references provide methods where the tissue and dendrimer compositions are brought into contact for the delivery of oligonucleotide. Regarding "active concentrations" in the phrase "contacting said tissue with said composition such that said biological agent is provided to said tissue at biologically active concentrations," it is noted that active concentration reads on any amount and since the prior art delivers oligonucleotide to tissues or cells, the prior art would meet any amount within the broad active concentrations claimed.

The combination of Foldvari and Baker discloses the use of dendrimers for the delivery of proteins or DNA. The combined reference failed to disclose the presence of polyester for the

delivery. But Park discloses polyesters as carriers for delivery of nucleic acids (abstract). Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the combined teaching of Foldvari and Baker for the delivery of DNA or protein. One having ordinary skill in the art would have been motivated to incorporate polyesters with dendrimer and expect to successfully deliver DNA.

Response to Arguments

4. Applicant's arguments filed 9/13/07 have been fully considered but they are not persuasive.

a) Applicant argues that the references in combination or alone do not teach skin patch membrane that is associated with at least one dendrimer and at least one biological agent comprising nucleic acid.

b) Applicant also argues that Foldvari does not teach the use of skin-patch membrane that is associated with at least one dendrimer and at least one biological agent comprising nucleic acid but that Foldvari teaches specific forms of transdermal delivery devices that do not include skin-patch membrane as required by the instant claims.

c) Applicant also argues that prior to the instant Examples 1-13, it was not known that skin patch membranes could effectively transfect nucleic acid associated with dendrimers so that one skilled in the art would not obtain sufficient guidance from the cited and that the examiner failed to provide the motivation to modify the transdermal delivery device of Foldvari to the skin patch membrane of the invention.

Response:

Claim 25 is a method that comprises a) providing a tissue such as skin cells and a composition that comprises a skin-patch membrane associated with at least one dendrimer and at least one biological agent comprising nucleic acid and b) contacting the tissue, that is the skin cell, with the composition such that the biological agent is provided to the tissue, which is the skin cell, with biologically active concentration. The claim does not say that the method involves transfection of nucleic acid associated with dendrimers by the use of skin patch.

With respect to the prior art, it is noted that Park discloses polyesters based dendrimers for delivery of oligonucleotides/nucleic acids (abstract) according to the description in the rejections above; Baker discloses the use of PAMAM dendrimers for the effective delivery of oligonucleotide/nucleic acids according to the description in the rejections above; Foldvari teaches transdermal delivery of DNA/nucleic acids/oligonucleotides (paragraph 4 of page 205). Transdermal delivery generally involves the use of a skin patch or membrane on the skin for the delivery of actives through the dermis into the blood stream and because the skin tissue has skin tissue cells, transdermal delivery involves the participation of skin tissue cells as evidenced by Banga et al. in vol. 16, issue 10, pp. 408-412 of the Trends in Biotechnology and by pages 1596 and 1597 of the 18th edition of Remington's Pharmaceutical Sciences, edited by Gennaro, 1990.

Therefore, regarding c), the claims are not directed to method of transfecting nucleic acid associated with dendrimers. Rather, one skilled in the art, would be motivated by the teaching of the references taken together to use transdermal delivery devices comprising polyester or PAMAM based dendrimers for delivery of nucleic acid/oligonucleotide/DNA via the skin of the subject by applying the transdermal device to the skin of the subject. The motivation comes from the combined teaching of the prior art whose goal is to deliver oligonucleotide by the use of

carrier materials such as polyester or PAMAM dendrimers. The motivation to combine the references also stems from the expected goal to deliver nucleic acid by transdermal administration. While applicant cites pages 203 to 204 of Foldvari as describing transdermal delivery devices that do not include skin permeation, it is noted that Foldvari on page 208 at paragraph 4 refers specifically to transdermal delivery of DNA and mentions the epidermis and stratum corneun, which are parts of the skin.

Regarding b) it is noted that skin patch membrane reads on transdermal delivery system and the references taken together teach a transdermal delivery device that comprises polyester or PAMAM dendrimers. Foldvari also discloses dendrimers that are complexed with DNA in spherical structures and the dendrimers and the DNA can be delivered to cell lines (right column, first full paragraph of page 205). Acrylate, PAMAM and polyethyleneimine polymers are some of the polymers listed that are used with the DNA (right column, page 205). Furthermore, Foldvari discloses the use of PLGA, PLA, lactides and glycolides for delivery of protein, carbohydrate or DNA vaccines (right column, page 204). These polymers are biocompatible and biodegradable. There is thus a reasonable expectation of success that the dendritic delivery systems of both Foldvari and Baker would deliver nucleic acid to the skin tissue cells by the transdermal process.

Therefore, regarding a) the cited references in combination teach transdermal delivery system comprising DNA associated with dendrimer where the DNA is at least one biological agent and the method of the claims is met when the transdermal delivery device containing the DNA-dendrimer is brought into contact with the skin tissue. The prior art is what is known in the prior art. The prior art teaches the ability to transdermally deliver nucleic acid before

applicant's invention according to the teaching of Foldvari. "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Applicant has not provided a showing that the nucleic acid cannot be delivered transdermally as taught by Foldvari, keeping in mind that transdermal delivery is topical and via skin tissue cells. It is known in the prior art that transdermal delivery utilizes patch that is topically affixed to the skin as evidenced by Banga et al. and the 18th edition of Remington's Pharmaceutical Sciences (see second full paragraph, page 6 above).

No claim is allowed.

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Blessing M. Fubara whose telephone number is (571) 272-0594. The examiner can normally be reached on 7 a.m. to 5:30 p.m. (Monday to Thursday).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Blessing Fubara
Patent Examiner
Tech. Center 1600

MICHAEL G. HARTLEY
SUPERVISORY PATENT EXAMINER